PHARMACEUTICAL ANALYSIS

UNIT 2 NOTES

ACID BASE TITRATION

- TITRATION
- ACID BASE TITRATION
- THEORIES OF INDICATORS
- NEUTRALIZATION CURVES

NON AQUEOUS TITRATION

- LEVELLING EFFECT
- ACIDIMETRY
- ALKALIMETRY
- ASSAY OF SODIUM BENZOATE

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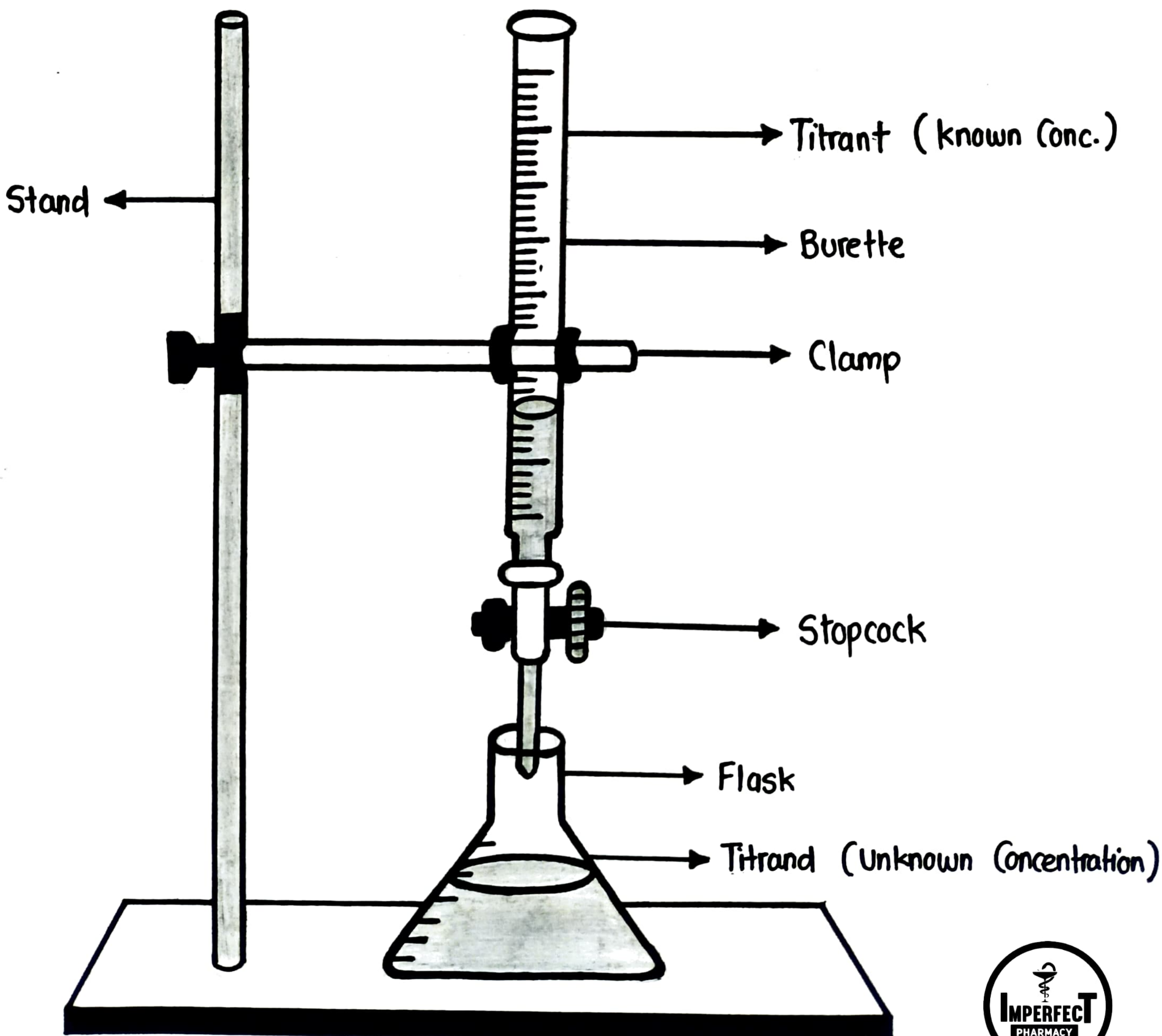
TITRATION

- Titration is also known as Titrimetry.
- Titration is a method of quantitative analysis in which we determine the concentration of an unknown solution with the help of a solution with known concentration. (Standard solution)
- Since volume plays an important role in titration, hence it is also known as Volumetric Analysis.



Types of Titration

- Acid- base Titration
- Redox Titration
- Precipitation Titration
- Complexometric Titration

Important terms in titration

Titrant : The solution of known concentration, always taken in burette.

Titrand : The solution of unknown concentration, always taken in flask also known as Analyte.

Equivalence Point : The point at which number of moles of analyte is equal to the number of moles of Titrant.

End Point : The point which shows the completion of titration at which the indicator shows the colour change. End point comes when one more drop of titrant is added in the analyte after equivalence point.

Indicators : These are the substance that are used in the titration for the determination of end point.

Titration Curve : It is a graph of pH of the analyte vs volume of the titrant added in the analyte / titrand.

ACID BASE TITRATION

- An acid- base titration is a quantitative analysis in which we determine the unknown concentration of an acid or base with the help of a known concentration of acid or base.
- Acid- base titration is also called Neutralization titration as it is based upon the neutralization reaction b/w acid & base.

Acidimetry

The determination of unknown concentration of a basic / alkaline solution by using a standard acidic solution is known as Acidimetry.

Alkalimetry

The determination of unknown concentration of an acidic solution by using a standard Basic / Alkaline solution is known as Alkalimetry.

Theories of Acid- Base Titration

- Arrhenius Theory
- Bronsted- Lowry Theory
- Lewis Theory
- Usanovich Theory
- Lux - Flood Theory

THEORIES OF INDICATORS

- An indicator is a substance which is used to determine the End Point in a titration.
- In acid base titrations, organic substances are generally used as Indicators.
- They change their colour within a certain pH range.

Theories :

There are basically two theories given to explain the colour changing nature of acid-base indicators

① Ostwald's Theory
② Quinonoid Theory

Ostwald's Theory

- According to the ostwald's theory indicators are generally weak acids or weak bases.
- The change in colour of the indicator is due to their ionisation.
- The unionised form of the indicator has different colour and Ionised form has different colour.

Unionised form (Different Colour)	⟷	Ionised Form (Different Colour)

- Now there can be two cases :

① Indicator is Weak Acid
② Indicator is Weak Base

If Indicator is Weak Acid

In case, if the indicator is a weak acid :

- Its ionisation in acids is very low due to common H^+ Ions, that means in acids it is in unionised form.
- It is fairly ionised in basic or alkaline solution, that means in bases it is in Ionised form.

example : Phenolphthalein is a weak acid indicator and it is represented by HPh

(Unionised) HPh	$\rightleftharpoons$	$H^+ + Ph^-$ (Ionised)
Colourless		Pink

If Indicator is Weak Base

In case, if the indicator is weak base :

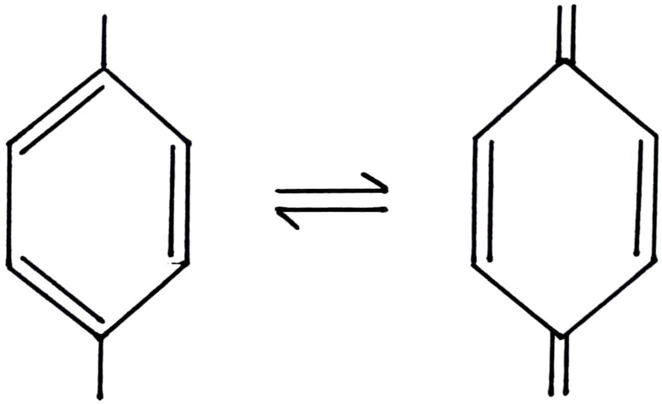
- Its ionisation is very low in bases due to common OH^- ions, that means in bases, it is in Unionised form.
- It is fairly ionised in acidic solution by H^+ ions, that means in acids it is in Ionised Form.

example : Methyl Orange is a weak base indicator and it is represented by MeOH

(Unionised) MeOH	$\rightleftharpoons$	$Me^+ + OH^-$ (Ionised)
Yellow		Red

Quinonoid Theory

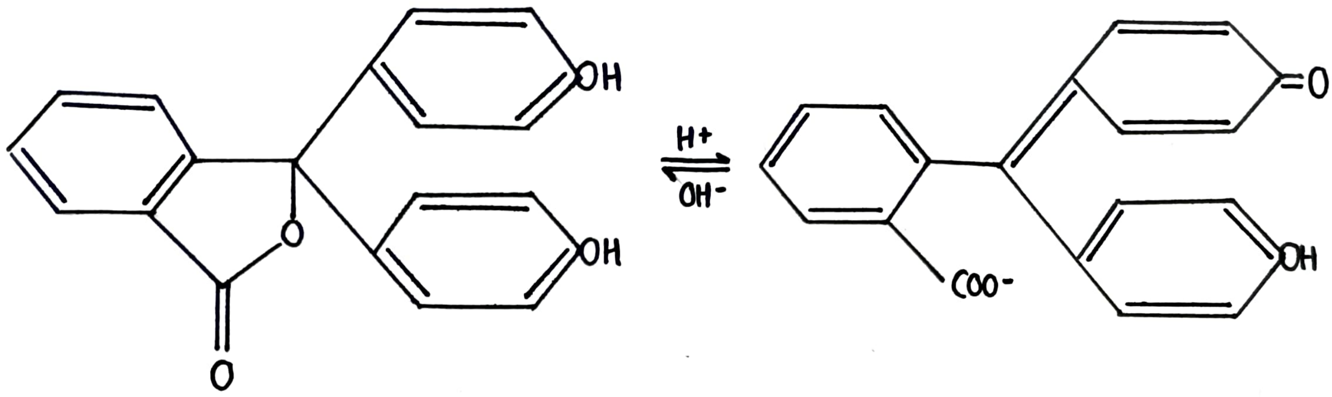
- According to quinonoid theory, an acid- base indicators exist in two tautomeric forms having different structures.
- One form is termed as Benzenoid Form and the other form is termed as Quinonoid Form.



Benzenoid Form　　　　Quinonoid Form

- The two forms have different colours
- One form exist in acidic medium and other in basic/ Alkaline medium.
- During titration, the medium changes from acidic to basic or vice-versa and due to this pH of solution is also changes which converts one tautomeric form into other and that's how colour changes.

Example: Phenolphthalein has benzenoid form in acidic medium which is colourless, while it has quinonoid form in alkaline medium which has pink colour.



Benzenoid Form of Phenolphthalein

Quinonoid Form of Phenolphthalein

Some Commonly Used Acid-Base Indicators:

No.	INDICATOR NAME	pH RANGE	ACID	BASE
1	Phenolphthalein	8.3 - 11.0	Colourless	Pink / Red
2	Methyl Orange	4 - 6	Red	Orange
3	Methyl Red	4.2 - 6.4	Red	Yellow
4	Phenol Red	6.4 - 8	Yellow	Red
5	Thymol Blue	1.2 - 2.8	Yellow / Red	Blue
6	Bromophenol Blue	3 - 4.6	Yellow	Blue

NEUTRALIZATION CURVES

- Neutralization curve is also known as Titration Curves.
- A Titration curve is a graph plot between pH of the analyte / Titrand vs volume of the Titrant added.
- As the equivalence point is reached in the titration, there is a rapid change in pH.

Some Important Terms in Neutralization Curves

Strong Acid

A Strong Acid is an acid which is completely dissociates when dissolved in water or aqueous solution.

$$HCl \longrightarrow H^+ + Cl^-$$

Weak Acid

A Weak Acid is an acid which do not completely dissociates when dissolved in water or aqueous solution.

$$CH_3COOH \rightleftharpoons CH_3COO^- + H^+$$

Strong Base

A Strong Base are those which completely dissociates when dissolved in water or aqueous solution.

$$NaOH \longrightarrow Na^+ + OH^-$$

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Weak Base : Weak base are those which do not completely dissociates when dissolved in water or aqueous solution.

$$NH_4OH \rightleftharpoons NH_4^+ + OH^-$$

Neutral Salt : A Neutral Salt is a product of strong Acid and strong Base reaction. pH of Neutral Salt = 7

$$HCl + NaOH \longrightarrow NaCl + H_2O$$

Acidic Salt : An acidic salt is a product of strong Acid and ~~Strong~~ Weak base reaction, pH of Acidic Salt < 7

$$HCl + NH_4OH \longrightarrow NH_4Cl + H_2O$$

Basic Salt : A basic salt is product of strong base and Weak Acid reaction. pH of basic salt > 7

$$CH_3COOH + NaOH \longrightarrow CH_3COONa + H_2O$$

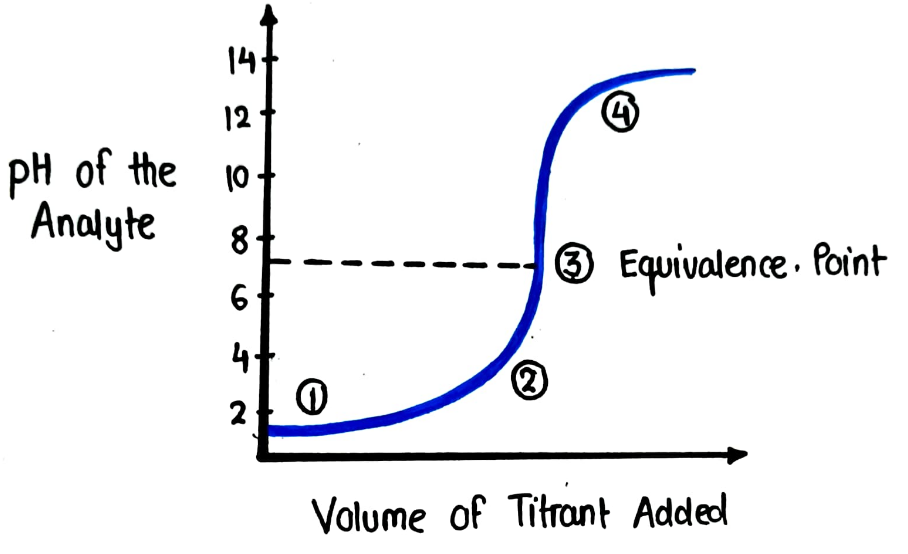
Classification of ACID - BASE Titrations

Acid base titrations are classified in four categories according to titration curve:

1. Strong Acid Vs Strong Base
2. Weak Acid vs Strong Base
3. Strong Acid vs Weak Base
4. Weak Acid vs Weak Base

Strong Acid vs Strong Base Titration

Suppose our analyte is hydrochloric acid (HCl) and Titrant is Sodium hydroxide (NaOH), that are strong acid and strong base. Now If we plot a graph between pH of the analyte vs volume of titrant added we will get a titration curve as shown below:



- **Point 1:** No NaOH is added in the HCl, so the pH of the analyte is very low due to strong acid. HCl

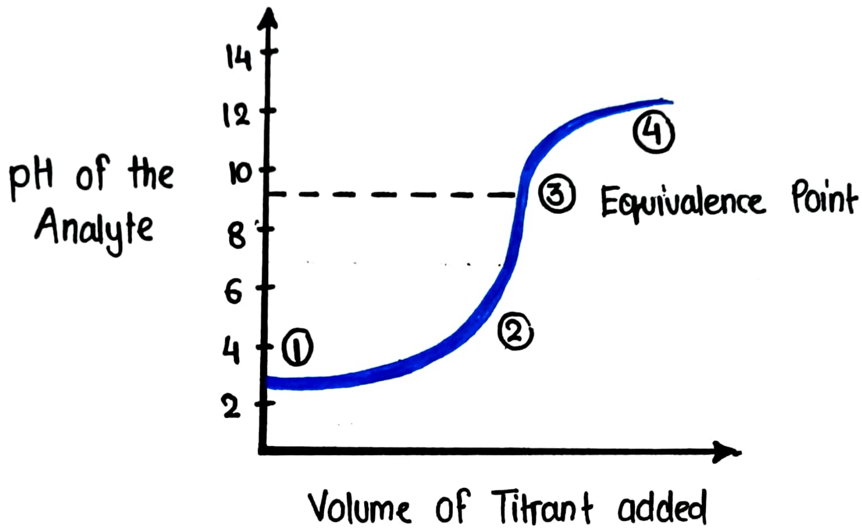
- **Point 2:** This is the point at which pH is recorded at a time just before complete neutralization takes place.

- **Point 3:** This is the equivalence point. A this time, moles of NaOH = moles of HCl in the analyte. The solution contains neutral salt and hence ph is neutral i.e. ph = 7

- **Point 4:** Addition of NaOH continues, pH starts becoming basic because HCl was neutralized at equivalence point and now excess of OH- ions present in the solution

Weak Acid Vs Strong Base Titration

Let's assume our analyte is acetic acid, CH_3COOH (Weak Acid) and Titrant is sodium hydroxide, NaOH (Strong base), now if we plot a graph b/w pH of the analyte (CH_3COOH) & volume of titrant (NaOH) added, then we will get a titration curve as shown below:



- **Point 1:** No ~~analyte is added in the~~ NaOH is added in the analyte so the pH of the analyte is low due to CH_3COOH

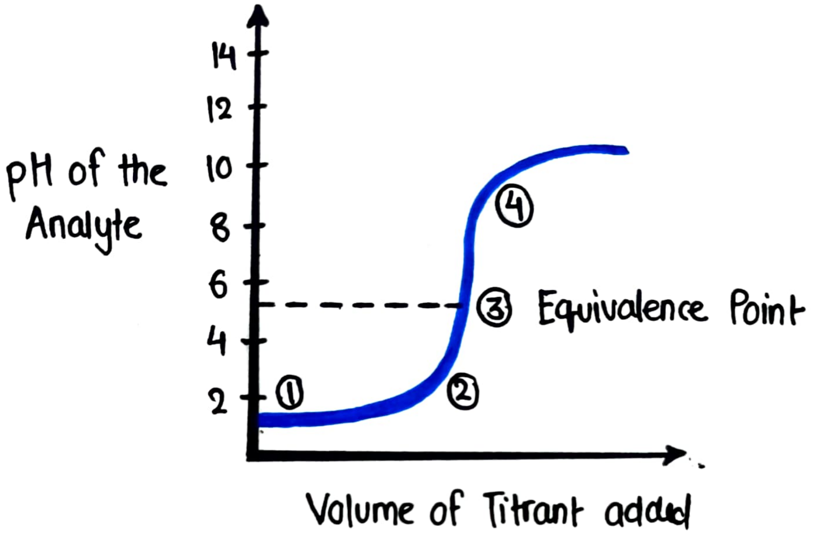
- **Point 2:** This is the pH recorded at a time just before complete neutralization takes place.

- **Point 3:** This is the equivalence point. At this time, moles of NaOH added = Moles of CH_3COOH, but since the reaction is between weak acid and strong base, the salt formed will be Basic Salt and hence pH is basic i.e., pH > 7

- **Point 4:** After equivalence point, pH will rises slowly & then become constant.

Strong Acid vs Weak Base Titration

Let's assume our analyte is hydrochloric acid HCl (strong acid) & titrant is Ammonium hydroxide NH_4OH (weak base), Now If we plot a graph b/w pH of the analyte (HCl) and volume of titrant (NH_4OH) added, then we will get a titration curve as shown below:-



- **Point 1 :** No NH_4OH is added in the analyte, so the pH of the analyte is very low due to strong acid HCl

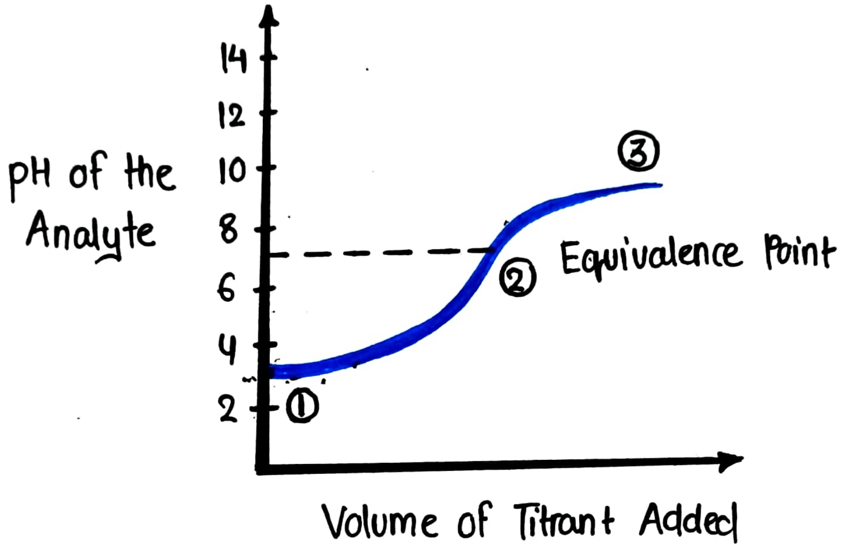
- **Point 2 :** This is the pH recorded at the time just before the complete neutralization takes place.

- **Point 3 :** This is the equivalence point, At this point moles of NH_4OH = Moles of HCl, but since the reaction is between strong acid and weak base, the salt formed will be acidic salt & pH will be acidic, i.e. $pH < 7$

- **Point 4 :** After, the equivalence point, NH_4OH addition continues & pH will increases.

Weak Acid vs Weak Base Titration

Let's assume our analyte is Acetic acid, CH_3COOH (weak acid) & Titrant is weak base, Ammonium hydroxide (NH_4OH), Now if we plot a graph b/w pH of the analyte & volume of titrant added, we will get a titration curve as shown below :-



Point 1 : No NH_4OH is added in the analyte, so the pH of the analyte will be low due to CH_3COOH.

Point 2 : At this point no of moles of CH_3COOH = no of moles of NH_4OH. equivalence point occurs at neutral pH, pH = 7

Point 3 : Since the titrant is weak base, hence it will not increase pH at a large extent.

NON AQUEOUS TITRATION

- Most of the titrations are performed in the aqueous media, means water is used as solvent, but in the case of weak acids and weak bases, use of water don't gives a sharp end point.
- Non-Aqueous solvents are those which do not contain water.
- Non-Aqueous Titration refers to a type of titration in which the analyte is dissolved in a solvent which doesn't contain water.

Reason For Non-Aqueous Titration

- The substance is insoluble in water.
- The substance is reactive with water
- The sample is too weak acid or too weak base.

Advantages of Non-Aqueous Titration

- Organic acids or bases that are insoluble in water are easily soluble in Non-aqueous solvent.
- It can be used for titration of mixture of acids as well.
- They are used for titration of weak acids and weak bases.
- Non-Aqueous Titrations are simple and accurate.

Disadvantages of Non-Aqueous Titrations

- Non-Aqueous solvents are generally expensive.
- Volatile solvent can pollute environment.
- Indicator must be prepare in Non-aqueous medium.

TYPES OF NON AQUEOUS SOLVENTS

There are basically 4 types of solvent used in the Non-aqueous Titration.

1. Protophilic Solvents
2. Protogenic Solvents
3. Amphoteric Solvents
4. Aprotic Solvents

Protophilic Solvents

- The word protophilic stands for 'proton lover'
- Protophilic solvents are basic in nature.
- They are used to dissolve acidic analytes
- They posses a high affinity for proton
- <u>examples</u> : Pyridine, amine etc.

Protogenic Solvents

- The word protogenic stands for 'Proton Generator'
- Protogenic solvents are acidic in nature & they can donate proton.
- They are used to dissolve basic analytes.
- They have dielectric constant.
- <u>examples</u> : Glacial acetic acid, Formic acid etc.

Amphiprotic Solvents

- They work as both protogenic and protophilic solvent.
- These solvents behave as acid as well as base.
- Amphiprotic solvents can either accept or donate the proton.
- <u>examples</u> : Alcohols, Methanol, Ethanol etc.

Aprotic Solvents

- These solvents are chemically inert.
- They are neither acidic or nor basic
- They do not accept or donate protons.
- They have low dielectric constant.
- examples: Benzene, Chloroform etc.

NOTE: The principle of Non Aqueous Titration is based on Bronsted- Lowry Theory of acid and base.

Most Commonly Used Non-Aqueous Solvent

- Glacial acetic acid
- Acetonitrile
- Alcohols
- Dioxane
- Dimethylformamid

LEVELLING EFFECT

- Levelling effect refers to the effect of solvents on the properties of acids and bases. It refers to increasing dissociation of compounds.
- Since all strong acids and bases are completely dissociates in water hence water has Levelling effect on strong acids and bases.

- But as we know weak acids and weak bases are hardly dissociates in water, hence water doesn't have a levelling effect on weak acids and weak bases

- The acidity of weak acids can be enhanced in the presence of basic (Protophilic) solvents. Weak acids behaves as strong acid in protophilic solvents, hence protophilic / basic solvents shows levelling effect on weak acids.

- The basicity of weak bases can be enhanced in the presence of acidic (protogenic) solvents. Weak bases behaves as strong base in protogenic solvents, hence protogenic solvents shows levelling effect on weak bases.

ALKALIMETRY

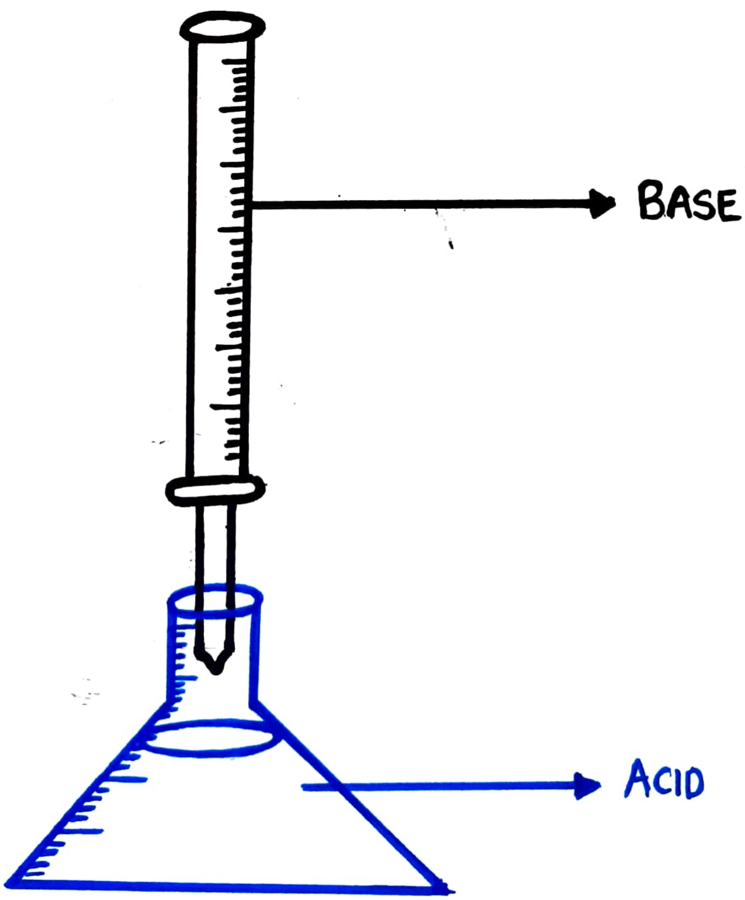
- Alkalimetry used to determine the concentration of acid substances using standard base.
- In alkalimetry a known volume of an acid is put into a conical flask and then titrated against standard solution of base taken in burette.
- Equivalent point is the point at which no. of moles of analyte (acid) is equal to the number of moles of titrant (base)

- Here in Alkalimetry

① Acid : Used as analyte taken in flask

② Base : Used as titrant taken in burette

- In, Alkalimetry, Base is the standard solution.

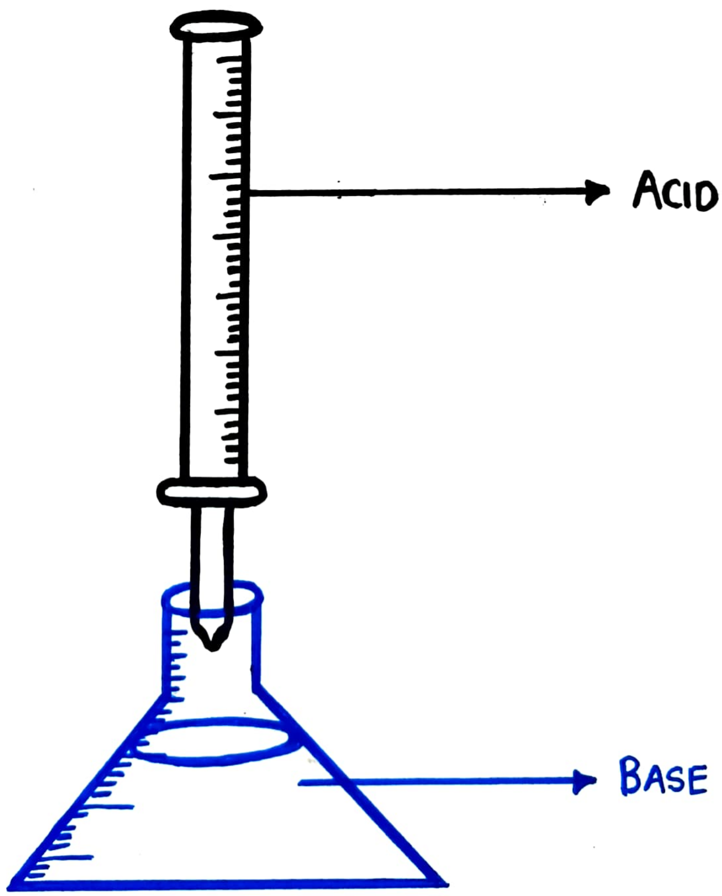


ACIDIMETRY

- Acidimetry used to determine the concentration of base substances using standard acid solution.
- In acidimetry, a known volume of a base is put into a conical flask, the solution is then titrated against a standard solution of acid taken in burette till equivalent point comes.
- Equivalent point is the point at which no. of moles of analyte (base) is equal to the no. of moles of titrant (acid).

- Here in acidimetry
① Acid : Used as Titrant taken in burette
② Base : Used as Analyte taken in flask

- In acidimetry, acid is the standard solution.



Types of Titration

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- Redox Titration
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- Complexometric Titration

Important terms in titration

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Indicators : These are the substance that are used in the titration for the determination of end point.

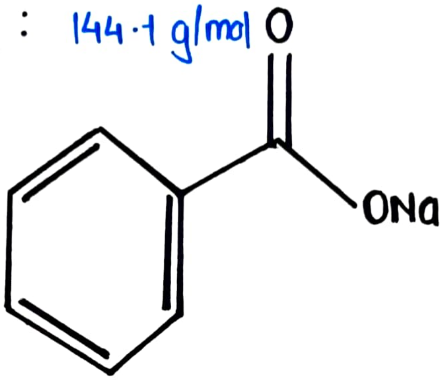
Titration Curve : It is a graph of pH of the analyte vs volume of the titrant added in the analyte / titrand.

ASSAY OF SODIUM BENZOATE

Molecular Formula : $C_7H_5NaO_2$

Molecular Weight : 144.1 g/mol

Structure :



Sodium benzoate contains not less than 99 % and not more than 100.5 % of $C_7H_5NaO_2$.

Principle

C_6H_5COONa + $HClO_4$ ⟶ C_6H_5COOH + $NaClO_4$

(Sodium benzoate) (Perchloric acid) (Benzoic acid) (Sodium Perchlora

Properties

- It is a white, crystalline or granular powder
- It is odourless.
- It is hygroscopic in nature.

Preparation and standardisation of 0.1 N Perchloric acid

Assay Of Sodium Benzoate

- Weight about 0.25 g of sodium benzoate and dissolve in 20 ml of anhydrous glacial acetic acid.
- If necessary then warm to 50°C and then cool
- Add crystal violet or 1- Naptholbenzein as indicator.
- Titrate with 0.1 N perchloric acid till colour changes to green.

Calculation

- 0.01441 g of C_6H_5COONa $\cong$ 1 ml of 0.1 N $HClO_4$

$$\% \text{ Purity of } C_6H_5COONa = \frac{\text{Vol. of } HClO_4 \times \text{N of } HClO_4 \times 0.01441}{\text{Weight of } C_6H_5COONa \times 0.1} \times 100$$

Uses

- Preservatives
- Additives etc.

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